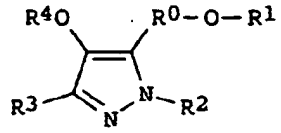

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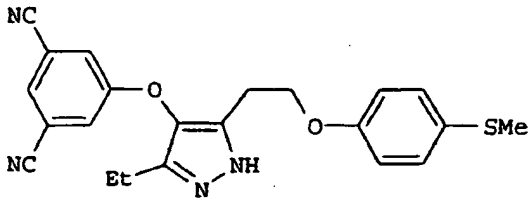

II

AB The title compds. [I; R0 = absent, alkylene; R1 = Ph substituted by SOyR5, alkylene(SOyR5), SOyCF3, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = H, alkyl, cycloalkyl, Ph, etc.; R4 = (un)substituted Ph, naphthyl, pyridyl; R5 = H, alkyl, cycloalkyl, etc.; y = 0-2] which bind to the enzyme reverse transcriptase and are modulators, especially inhibitors thereof, and as such are useful in the treatment of a variety of disorders including those in which the inhibition of reverse transcriptase is implicated, were prepared and formulated. Disorders of interest include those caused by Human Immunodificiency Virus (HIV) and genetically related retroviruses, such as Acquired Immune Deficiency Syndrome (AIDS). Thus, reacting 5-{[3-ethyl-5-(2-hydroxyethyl)-1H-pyrazol-4-yl]oxy}isophthalonitrile (preparation given) with 4-(methylmercapto)phenol afforded I [R0 = (CH2)2; R1 = 4-(MeS)C6H4; R2 = H; R3 = Et; R4 = 3,5-(NC)2C6H3] which showed IC50 of 2 nM against HIV-1 reverse transcriptase. The pharmaceutical composition comprising the compound I is claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:832763 CAPLUS
DOCUMENT NUMBER: 137:337884
TITLE: Preparation of aryloxy pyrazole derivatives as reverse transcriptase inhibitors for treating HIV
INVENTOR(S): Jones, Lyn Howard; Mowbray, Charles Eric; Price, Davis Anthony; Selby, Matthew Duncan; Stupple, Paul Anthony
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085860	A1	20021031	WO 2002-IB1234	20020404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2443449	AA	20021031	CA 2002-2443449		20020404
EP 1377556	A1	20040107	EP 2002-708600		20020404
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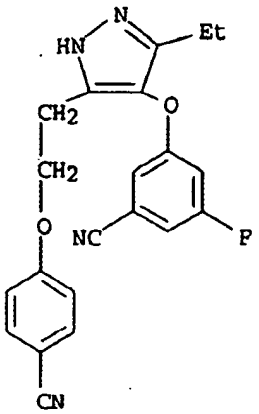
EE 200300497	A	20040216	EE 2003-497		20020404
BR 2002008811	A	20040309	BR 2002-8811		20020404
JP 2004531535	T2	20041014	JP 2002-583387		~~20020404~~
US 2003100554	A1	20030529	US 2002-118512		20020405
ZA 2003007095	A	20040910	ZA 2003-7095		~~20030910~~
NO 2003004523	A	20031209	NO 2003-4523		20031009
PRIORITY APPLN. INFO.:			GB 2001-8999	A	20010410
			GB 2001-27426	A	20011115
			US 2001-289570P	P	20010508
			US 2002-346727P	P	20020107
			WO 2002-IB1234	W	20020404

OTHER SOURCE(S): MARPAT 137:337884

IT **473921-42-5P**, 3-[[5-[2-(4-Cyanophenoxy)ethyl]-3-ethyl-1H-pyrazol-4-yl]oxy]-5-fluorobenzonitrile **473921-43-6P**, 3-Fluoro-5-[[3-ethyl-5-(2-((2-methyl-3-pyridyl)oxy)ethyl)-1H-pyrazol-4-yl]oxy]benzonitrile **473921-44-7P**, 3-Fluoro-5-[[3-ethyl-5-(2-((3-pyridyl)oxy)ethyl)-1H-pyrazol-4-yl]oxy]benzonitrile **473921-45-8P**, 3-Fluoro-5-[[3-ethyl-5-(2-((2-amino-3-pyridyl)oxy)ethyl)-1H-pyrazol-4-yl]oxy]benzonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aryloxy pyrazole derivs. as reverse transcriptase inhibitors for treating HIV)

RN 473921-42-5 CAPLUS

CN Benzonitrile, 3-[[5-[2-(4-cyanophenoxy)ethyl]-3-ethyl-1H-pyrazol-4-yl]oxy]-5-fluoro- (9CI) (CA INDEX NAME)



RN 473921-43-6 CAPLUS

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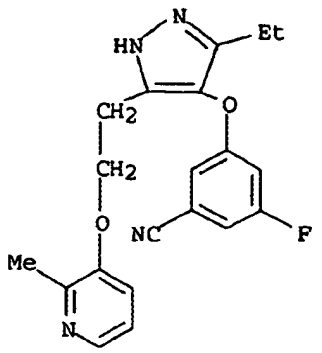

RN 473921-44-7 CAPLUS
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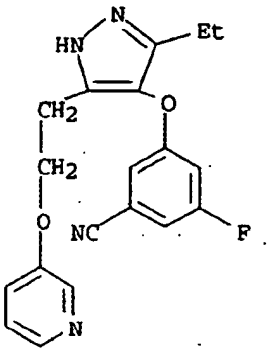

RN 473921-45-8 CAPLUS
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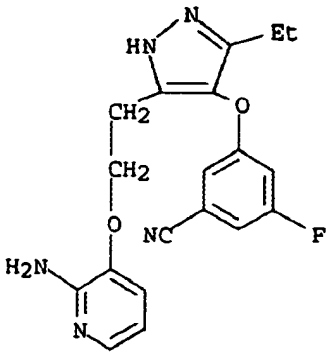
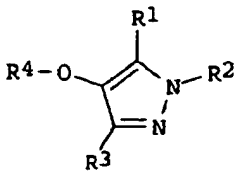


GI



I

AB This invention relates to pyrazole derivs. (shown as I; e.g. 2-Amino-6-[[4-(3,5-dichlorophenoxy)-3,5-diethyl-1H-pyrazol-1-yl]methyl]-4(3H)-pyrimidinone) or pharmaceutically acceptable salts, solvates or derivative thereof, wherein R1 to R4 are defined below, and to processes for the preparation thereof, intermediates used in their preparation of, compns. containing them and the uses of such derivs. The compds. of the present invention bind to the enzyme reverse transcriptase and are modulators, especially inhibitors thereof. As such the compds. of the present invention are useful in the treatment of a variety of disorders including those in which the inhibition of reverse transcriptase is implicated. Disorders of interest include those caused by Human Immunodeficiency Virus (HIV) and genetically related retroviruses, such as Acquired Immune Deficiency Syndrome (AIDS). In tests of inhibition of HIV-1 reverse transcriptase enzyme, the claimed compds. 2-amino-6-[[4-(3,5-dichlorophenoxy)-3,5-diethyl-1H-pyrazol-1-yl]methyl]-4(3H)-pyrimidinone, 3,5-dimethyl-4-[[3,5-diethyl-1-(2-hydroxyethyl)-1H-pyrazol-4-yl]oxy]benzonitrile and 1-(3-azetidinyl)-4-(3,5-dichlorophenoxy)-3,5-diethyl-1H-pyrazole had IC50 values of 39,000, 3,200 and 248 nM, resp. In I: R1 is H, C1-C6 alkyl, C3-C7 cycloalkyl, Ph, benzyl, halo, -CN, -OR7, -CO2R10, -CONR5R10, R8 or R9. R2 is H, C1-C6 alkyl, C3-C6 alkenyl, C3-C6 alkynyl, C3-C7 cycloalkyl, C3-C7 cycloalkenyl, Ph, benzyl, R8 or R9; or, R1 and R2, when taken together, represent unbranched C3-C4 alkylene. R3 is H, C1-C6 alkyl, C3-C7 cycloalkyl, Ph, benzyl, halo, -CN, -OR7, -CO2R5, -CONR5R5, R8 or R9; R4 is Ph, naphthyl or pyridyl. Definitions of R5 and R7-R10 and addnl. specifications are given in the claims. Included are 283 claimed-compound prepns. and 115 intermediate prepns.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.58	516.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.46	-3.65

FILE 'REGISTRY' ENTERED AT 19:19:48 ON 15 APR 2005
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